We Claim:

1. A method for determining renal toxicity in an individual comprising:

(a) obtaining a body sample from said individual,

(b) determining from the body sample the level of gene expression corresponding to one or more genes selected among Calbindin-D28k, KIM-1, OPN, EGF and Clusterin, to obtain a first set of value, and

(c) comparing the first set of value with a second set of value corresponding to the level of gene expression assessed for the same gene(s) and under identical condition as for step b) in a body sample of an individual not subject to renal toxicity, wherein the first value lower than the second value for Calbindin-D28K and/or EGF gene expression is an indication that the individual of step a) is having, developing or sensitive to renal toxicity, and/or wherein the first value greater than the second value for KIM-1, Osteopontin and/or Clusterin gene expression is an indication that the individual is having, developing or sensitive to renal toxicity.

2. The method of claim 1, wherein in steps b) and c) at least 2 or 3 genes selected among Calbindin-D28k, KIM-1, OPN, EGF and Clusterin are used.

3. A method for determining renal toxicity in an individual comprising:

(a) obtaining a body sample from an individual,

(b) determining from the body sample the level of gene expression corresponding to one or more genes selected among Alpha-2u globulin related-protein (Alpha-2u), Complement component 4 (C4), Vascular Endothelial Growth Factor (VEGF), Kidney-specific Organic Anion Transporter-K1 (OAT-K1), Aldolase A, Aldolase B and Podocin, to obtain a first set of value, and

(c) comparing the first set of value with a second set of value corresponding to the level of gene expression assessed for the same gene(s) and under identical condition as for step b) in a body sample of an individual not subject to renal toxicity, wherein the first value lower than the second value for VEGF, OAT-K1, Aldolase A, Aldolase B and/or Podocin gene expression is an indication that the individual of step a) is having, developing or sensitive to renal toxicity, and/or wherein the first value greater than the second value for Alpha-2u and/or C4 gene expression is an indication that the individual is having, developing or sensitive to renal toxicity.

4. The method of claim 3, wherein in steps b) and c) at least 2 or 3 genes selected among VEGF, OAT-K1, Aldolase A, Aldolase B, Podocin, Alpha-2u and C4 are used.

5. A method of claim 1 and 3, wherein in steps b) and c) at least 2 or 3 genes selected among Calbindin-D28k, KIM-1, OPN, EGF, Clusterin, VEGF, OAT-K1, Aldolase A, Aldolase B, Podocin, Alpha-2u and C4 are used.

6. A method for determining renal toxicity in an individual under treatment with a cytotoxic agent comprising:

(a) obtaining a body sample from said individual,

(b) determining from the body sample the level of gene expression corresponding to one or more genes selected among Calbindin-D28k, KIM-1, OPN, EGF, Clusterin Alpha-2u, C4, VEGF, OAT-K1, Aldolase A, Aldolase B and Podocin, to obtain a first set of value, and

(c) comparing the first set of value with a second set of value corresponding to the level of gene expression assessed for the same gene(s) and under identical condition as for step b) in a body sample of an individual not subject to renal toxicity, wherein the first value lower than the second value for Calbindin-D28K, EGF, VEGF, OAT-K1, Aldolase A, Aldolase B and/or Podocin gene expression is an indication that the individual of step a) is having, developing or sensitive to renal toxicity, and/or wherein the first value greater than the second value for KIM-1, OPN, Clusterin, Alpha-2u and/or C4 gene expression is an indication that the individual is having, developing or sensitive to renal toxicity.

7. The method of claim 6, wherein the cytotoxic agent is selected among cyclosporine, cisplatin, tacrolimus, aminoglycosides, sulfonamides and trimethadione.

8. A method of claim 6 or 7, wherein in steps b) and c) at least 2 or 3 genes selected among Calbindin-D28k, KIM-1, OPN, EGF, Clusterin, VEGF, OAT-K1, Aldolase A, Aldolase B, Podocin, Alpha-2u and C4 are used.

9. The method of any one of claims 1 to 8, wherein mRNA expression levels in the body sample of the individual of step b), of Calbindin-D28k below 5.30E+08, of KIM-1 above 1.50E+07, of EGF below 2.80E+08, of Osteopontin above 1.40E+08, of Clusterin above 1.90E+09, and/or podocin below 3.00E+06, indicates that such individual is having, developing or sensitive to renal toxicity, wherein mRNA expression levels are expressed in absolute value.

10. The method of any one of claims 1 to 8, wherein a repression of at least 4 fold for EGF, of at least 2 fold for VEGF, of at least 2 fold for OAT-K1, of at least 20 fold for Aldolase A, and/or for Aldolase B of at least 2 fold, and/or wherein an induction of at least 20 fold for KIM-1, of at least 3 fold for OPN, of at least 7 fold for Clusterin, of at least 50 fold for Alpha-2u and/or for C4 of at least 3 fold is an indication that such individual is having, developing or sensitive to renal toxicity.

11. The method of claims 1 to 10, wherein the level of gene expression is assessed by detecting the presence of a protein corresponding to the gene expression product.

12. A test for use in determining whether a renal toxicity in an individual will respond to therapy comprising the steps of, performing steps a), b) and c) set forth in one of the claims 1 to 11 for a body sample obtained from an individual treated against renal toxicity with a pharmaceutically acceptable agent and determining the responsiveness of the individual to drug therapy.

13. A method for treating renal toxicity in an individual comprising the step of administering to said individual a therapeutically effective amount of a modulating compound that modulates in the kidney the synthesis, expression or activity of one or more of the genes or gene expression products of the group of genes Calbindin-D28k, KIM-1, OPN, EGF and/or Clusterin, so that at least one symptom of renal toxicity is ameliorated.

14. A method of claim 13, wherein after treatment with the modulating compound the renal toxicity of the individual is determined according to claims 1, 2, or 5 to 8, and wherein gene mRNA expression levels in a body sample of the individual, of Calbindin-D28k above 5.30E+08, of KIM-1 below 1.50E+07, of EGF above 2.80E+08, of Osteopontin below 1.40E+08, and/or of Clusterin below 1.90E+09, indicates that at least one symptom of renal toxicity is ameliorated, wherein gene mRNA expression levels are expressed in absolute value.

15. A method for treating renal toxicity in an individual comprising the step of administering to said individual a therapeutically effective amount of a modulating compound that modulates in the kidney the synthesis, expression or activity of one or more of the genes or gene expression products of the group of genes VEGF, OAT-K1, Aldolase A, Aldolase B, Podocin, Alpha-2u and/or C4, so that at least one symptom of renal toxicity is ameliorated.

16. The method of claim 13 or 15, wherein after treatment with the modulating compound the renal toxicity of the individual is determined according to of any one of claims 1 to 11, wherein a repression of gene expression of less than 4 fold for EGF, of less than 2 fold for VEGF, of less than 2 fold for OAT-K1, of less than 20 fold for Aldolase A, and/or for Aldolase B of less than 2 fold, and/or wherein an induction of gene expression of less than 20 fold for KIM-1, of less than 3 fold for OPN, of less than 7 fold for Clusterin, of less than 50 fold for Alpha-2u and/or for C4 of less than 3 fold indicates that at least one symptom of renal toxicity is ameliorated.

17. A method for treating renal toxicity in an individual under treatment with a cytotoxic agent comprising the step of administering to said individual a therapeutically effective amount of a modulating compound that modulates in the kidney the synthesis, expression or activity of one or more of the genes or gene expression products of the group of genes Calbindin-D28k, KIM-1, OPN, EGF, Clusterin, VEGF, OAT-K1, Aldolase A, Aldolase B, Podocin, Alpha-2u and/or C4 so that at least one symptom of renal toxicity is ameliorated.

18. The method of claim 17, wherein the cytotoxic agent is selected among cyclosporine, cisplatin, tacrolimus, aminoglycosides, sulfonamides and trimethadione.

19. A method for identifying candidate agents for use in the treatment of renal toxicity comprising the steps of:

(a) contacting a sample of a kidney tissue subject to toxicity with a candidate agent,

(b) determining from the kidney tissue the level of gene expression corresponding to one or more genes selected among Calbindin-D28k, KIM-1, OPN, EGF and Clusterin, to obtain a first set of value, and

(c) comparing the first set of value with a second set of value corresponding to the level of gene expression assessed for the same gene(s) and under identical condition as for step b) in a kidney tissue subject to toxicity not induced by the candidate agent wherein a first value substantially greater than the second value for Calbindin-D28K and/or EGF gene expression is an indication that the candidate agent is ameliorating renal toxicity symptoms, and/or wherein a first value substantially lower than the second value for KIM-1, Osteopontin and/or Clusterin gene expression is an indication that the candidate agent is ameliorating renal toxicity symptoms.

20. The method of claim 19, wherein in steps b) and c) at least 2 or 3 genes selected among Calbindin-D28k, KIM-1, OPN, EGF and Clusterin are used.

21. A method for identifying candidate agents for use in the treatment of renal toxicity comprising the steps of:

(a) contacting a sample of a kidney tissue subject to toxicity with a candidate agent,

(b) determining from the kidney tissue the level of gene expression corresponding to one or more genes selected among VEGF, OAT-K1, Aldolase A, Aldolase B, Podocin, Alpha-2u and C4, to obtain a first set of value, and

(c) comparing the first set of value with a second set of value corresponding to the level of gene expression assessed for the same gene(s) and under identical condition as for step b) in a kidney tissue subject to toxicity not induced by the candidate agent wherein a first value substantially greater than the second value for VEGF, OAT-K1, Aldolase A, Aldolase B and/or Podocin gene expression is an indication that the candidate agent is ameliorating renal toxicity symptoms, and/or wherein a first value substantially lower than the second value for Alpha-2u and/or C4 gene expression is an indication that the candidate agent is ameliorating renal toxicity symptoms.

22. The method of claim 21, wherein in steps b) and c) at least 2 or 3 genes selected among VEGF, OAT-K1, Aldolase A, Aldolase B, Podocin, Alpha-2u and C4 are used.

23. A method of claim 19 or 21, wherein in steps b) and c) at least 2 or 3 genes selected among Calbindin-D28k, KIM-1, OPN, EGF, Clusterin, VEGF, OAT-K1, Aldolase A, Aldolase B, Podocin, Alpha-2u and C4 are used.

24. The method of claim 19, 20 or 23, wherein mRNA gene expression level in kidney tissue subject to toxicity, of Calbindin-D28k above 5.30E+08, of KIM-1 below 1.50E+07, of EGF above 2.80E+08, of Osteopontin below 1.40E+08, of Clusterin below 1.90E+09, and/or of Podocin above 3.00E+06 is an indication that the candidate agent is ameliorating renal toxicity, wherein mRNA gene expression level is expressed in absolute value.

25. The method of any one of claims 19 to 23, wherein a repression of gene expression of less than 4 fold for EGF, of less than 2 fold for VEGF, of less than 2 fold for OAT-K1, of less than 20 fold for Aldolase A, and/or for Aldolase B of less than 2 fold, and/or wherein an induction gene expression of less than 20 fold for KIM-1, of less than 3 fold for OPN, of less than 7 fold for Clusterin, of less than 50 fold for Alpha-2u and/or for C4 of less than 3 fold is an indication that the candidate agent is ameliorating renal toxicity.

26. The method of claims 19 to 25, wherein the level of gene expression is assessed by detecting the presence of a protein corresponding to the gene expression product.

27. A method for identifying candidate agents that do not provoke or induce renal toxicity comprising the steps of:

a) contacting a sample of a kidney tissue not subject to toxicity with a candidate agent,

b) determining from the kidney tissue the level of gene expression corresponding to one or more genes selected among Calbindin-D28k, KIM-1, OPN, EGF and Clusterin, to obtain a first set of value, and

c) comparing the first set of value with a second set of value corresponding to the level of gene expression assessed for the same gene(s) and under identical condition as for step b) in a kidney tissue not subject to toxicity, wherein a first value equal or higher than the second value for Calbindin-D28K and/or EGF gene expression is an indication that the candidate agent does not provoke or induce renal toxicity, and/or wherein a first value equal or lower than the second value for KIM-1, Osteopontin and/or Clusterin gene expression is an indication that the candidate agent does not provoke or induce renal toxicity.

28. The method of claim 27, wherein in steps b) and c) at least 2 or 3 genes selected among Calbindin-D28k, KIM-1, OPN, EGF and Clusterin are used.

29. A method for identifying candidate agents that do not provoke or induce renal toxicity comprising the steps of:

a) contacting a sample of a kidney tissue not subject to toxicity with a candidate agent,

b) determining from the kidney tissue the level of gene expression corresponding to one or more genes selected among VEGF, OAT-K1, Aldolase A, Aldolase B, Podocin, Alpha-2u and C4, to obtain a first set of value, and

c) comparing the first set of value with a second set of value corresponding to the level of gene expression assessed for the same gene(s) and under identical condition as for step b) in a kidney tissue not subject to toxicity, wherein a first value equal or higher than the second value for VEGF, OAT-K1, Aldolase A, Aldolase B, and/or Podocin, gene expression is an indication that the candidate agent does not provoke or induce renal toxicity, and/or wherein a first value equal or lower than the second value for

Alpha-2u and/or C4 gene expression is an indication that the candidate agent does not provoke or induce renal toxicity.

30. The method of claim 29, wherein in steps b) and c) at least 2 or 3 genes selected among VEGF, OAT-K1, Aldolase A, Aldolase B, Podocin, Alpha-2u and C4 are used.

31. A method of claim 27 or 29, wherein in steps b) and c) at least 2 or 3 genes selected among Calbindin-D28k, KIM-1, OPN, EGF, Clusterin, VEGF, OAT-K1, Aldolase A, Aldolase B, Podocin, Alpha-2u and C4 are used.

32. The method of claims 27, 28 or 31, wherein mRNA expression level determined in the kidney tissue not subject to toxicity, of Calbindin-D28k above 5.30E+08, of KIM-1 below 1.50E+07, of EGF above 2.80E+08, of Osteopontin below 1.40E+08, of Clusterin below 1.90E+09 and/or of Podocin above 3.00E+06, is an indication that the candidate agent does not provoke or induce renal toxicity, wherein mRNA expression level is expressed in absolute value.

33. The method of any one of claims 27 to 31, wherein a repression of gene expression of less than 4 fold for EGF, of less than 2 fold for VEGF, of less than 2 fold lower for OAT-K1, of less than 20 fold lower for Aldolase A, and/or for Aldolase B of less than 2 fold lower than the second value, and/or wherein an induction of gene expression of less than 20 fold for KIM-1, of less than 3 fold for OPN, of less than 7 fold for Clusterin, of less than 50 fold for Alpha-2u and/or for C4 of less than 3 fold is an indication that the candidate agent does not provoke or induce renal toxicity.

34. The method of claims 27 to 33 wherein the level of gene expression is assessed by detecting the presence of a protein corresponding to the gene expression product.

35. The method of claims 27 to 34 wherein the method is performed *in vitro*, and the kidney tissue subject to toxicity is obtained from a cultured kidney tissue contacted with a cytotoxic agent under cytotoxic conditions.

36. The method of claims 27 to 35 wherein the kidney tissue subject to toxicity is a kidney sample of an individual subject to renal toxicity, said sample having mineralization, fibrosis, tubular, infiltration, necrosis damages or any other kind of damages that results in renal dysfunction.

37. A method for comparing renal cytotoxic potentials of two drug candidates comprising the steps of:

a) contacting a sample of a kidney tissue not subject to toxicity with a first drug candidate, and determining from the kidney tissue the level of gene expression corresponding to one or more genes selected among Calbindin-D28k, KIM-1, OPN, EGF and Clusterin, to obtain a first set of value, and

b) contacting a sample of a kidney tissue not subject to toxicity with a second drug candidate, and determining from the kidney tissue level(s) of gene expression(s) corresponding to one or more genes selected among Calbindin-D28k, KIM-1, OPN, EGF and Clusterin, to obtain a second set of value, and

c) comparing the first set of value to the second set of value, wherein if the first value is substantially lower than the second value for Calbindin-D28K and/or EGF gene expression this is an indication that the second drug candidate is less cytotoxic to the kidney than the second drug candidate, and/or wherein if the first value is substantially higher than the second value for KIM-1, Osteopontin and/or Clusterin gene expression this is an indication that the second drug candidate is less cytotoxic to the kidney than the second drug candidate.

38. A method for comparing renal cytotoxic potentials of two drug candidates comprising the steps of:

a) contacting a sample of a kidney tissue not subject to toxicity with a first drug candidate, and determining from the kidney tissue the level of gene expression corresponding to one or more genes selected among VEGF, OAT-K1, Aldolase A, Aldolase B, Podocin, Alpha-2u and C4, to obtain a first set of value, and

b) contacting a sample of a kidney tissue not subject to toxicity with a second drug candidate, and determining from the kidney tissue level(s) of gene expression(s) corresponding to one or more genes selected among VEGF, OAT-K1, Aldolase A, Aldolase B, Podocin, Alpha-2u and C4, to obtain a second set of value, and

c) comparing the first set of value to the second set of value, wherein if the first value is substantially lower than the second value for VEGF, OAT-K1, Aldolase A, Aldolase B, and/or Podocin gene expression this is an indication that the second drug candidate is less cytotoxic to the kidney than the second drug candidate, and/or wherein if the first value is substantially higher than the second value for Alpha-2u and/or C4 gene

expression this is an indication that the second drug candidate is less cytotoxic to the kidney than the second drug candidate.

39. The method according to the preceding claims wherein the level of expression of mRNA is detected by techniques selected from the group consisting of Northern blot analysis, reverse transcription PCR and real time quantitative PCR, branched DNA, nucleic acid sequence based amplification (NASBA), transcription-mediated amplification, ribonuclease protection assay, or any other methods for gene expression analysis currently available or that are to come.

40. The use of some polymorphism in a gene for the diagnostic of renal toxicity, wherein the gene is chosen from Calbindin-D28k, KIM-1, OPN, EGF and Clusterin.

41. The use of a polymorphism in a gene for the diagnostic of renal toxicity, wherein the gene is chosen from VEGF, OAT-K1, Aldolase A, Aldolase B, Podocin, Alpha-2u and C4.

42. The use of a polymorphism in a gene for the diagnostic of renal toxicity, wherein the gene is chosen from Calbindin-D28k, KIM-1, OPN, EGF, Clusterin, VEGF, OAT-K1, Aldolase A, Aldolase B, Podocin, Alpha-2u and C4.

43. A kit for diagnosing renal toxicity in an individual comprising a means for determining the level of gene expression corresponding to one or more marker genes selected among Calbindin-D28k, KIM-1, OPN, EGF, Clusterin, VEGF, OAT-K1, Aldolase A, Aldolase B, Podocin, Alpha-2u and C4.

44. A kit according to claim 43, wherein the individual is under treatment with a cytotoxic agent.

45. A kit according to claim 43 or 44, wherein the expression of at least 2 or 3 marker genes selected among Calbindin-D28k, KIM-1, OPN, EGF, Clusterin, VEGF, OAT-K1, Aldolase A, Aldolase B, Podocin, Alpha-2u and C4 can be determined.

46. A kit according to any of claims 43 to 45, wherein the means for determining the level of gene expression comprise one or more oligonucleotides specific for a marker gene.

47. A kit according to any of claims 43 to 46, wherein the means for determining the level of gene expression comprise methods selected from Northern blot analysis, reverse transcription PCR or real time quantitative PCR, branched DNA, nucleic acid

sequence based amplification (NASBA), transcription-mediated amplification, ribonuclease protection assay, and microarrays.

48. A kit according to any of claims 43 to 45, wherein the means for determining the level of gene expression comprise at least one antibody specific for a protein encoded by the marker gene selected among Calbindin-D28k, KIM-1, OPN, EGF, Clusterin, VEGF, OAT-K1, Aldolase A, Aldolase B, Podocin, Alpha-2u and C4.

49. A kit according to claim 48, wherein the antibody is selected among polyclonal antibodies, monoclonal antibodies, humanized or chimeric antibodies, and biologically functional antibody fragments sufficient for binding of the antibody fragment to the marker.

50. A kit according to any of claims 48 or 49, wherein the means for determining the level of gene expression comprise an immunoassay method.

51. A kit according to any of claims 43 to 50, further comprising means for obtaining a body sample of the individual.

52. A kit according to any of claims 43 to 51, further comprising a container suitable for containing the means for determining the level of gene expression and the body sample of the individual.

53. A kit according to any of claims 43 to 52, further comprising instructions for use and interpretation of the kit results.

54. A method for identifying a candidate gene associated with a biological process including kidney function, renal toxicity, and/or kidney disorders comprising:

a) using a gene expression level of at least one marker selected among Calbindin-D28k, KIM-1, OPN, EGF, Clusterin, VEGF, OAT-K1, Aldolase A, Aldolase B, Podocin, Alpha-2u and C4 as input for an algorithm for obtaining at least one numerical value I;

b) comparing the at least one numerical value I obtained in a) with a numerical value II obtained for the candidate gene.

55. A method of claim 54, further comprises step c), wherein the candidate gene is associated with the biological process if the value I obtained in step b) correlates in a predetermined relationship to value II.

56. The method of claims 54 or 55, wherein the predetermined relationship is 1 or greater.

57. The method of claims 54 or 55, wherein the predetermined relationship is 1 or less.

58. A method of any of claims 54 to 57, wherein the gene expression levels of the at least one marker selected among Calbindin-D28k, KIM-1, OPN, EGF, Clusterin, VEGF, OAT-K1, Aldolase A, Aldolase B, Podocin, Alpha-2u and C4 is obtained from a different body sample of an individual such as kidney tissue, blood or urine or from a cell line such as a kidney cell line.

59. The method of any of claims 54 to 58, wherein the body sample or the cell line have been in contact with a cytotoxic agent.

60. The method of any of claims 54 to 59, wherein the method is a computer-executable method.